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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,159	04/25/2001	Yin Luo	A-68292-2/RMS/DHR	8575

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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 04/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/843,159	LUO ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-26 and 31-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12, 16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1- 37 are still at issue and are present for examination. Claims 27-30 are now under consideration. Claims 1-26, 31-37 remain withdrawn from consideration as being directed to non-elected invention.

Election/Restrictions

Applicant's election with traverse of Group IX, Claims 27-30 in Paper No. 15 is acknowledged. The traversal is on the ground(s) that coexamination of all of Groups III and IX and claim 8 would not require independent searches or cause undue burden on the Examiner. This is not found persuasive because while the searches for the three groups appear to overlap, they are not coextensive. The search for Groups III would each require the search of subclasses unnecessary for the search of elected Group IX. Furthermore the search also requires extensive non-patent literature. The groups are patentably distinct from each other as explained in the previous Office action as they are methods which have different steps and arrive at different results even though there may be slight overlap of the steps.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-26 and 31-37 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 15.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 27 recites an abbreviation for a protein "TaHo" without providing an expansion for the same. Examiner requests that applicants expand the above abbreviation to overcome this rejection.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 28 recites the phrase "small molecule". The metes and bounds of the term "small" is not clear to the Examiner. While the phrase 'small molecules" is known to the Examiner, it is not clear to the Examiner as to at what is the range of molecular weights of a given set of compounds that applicants consider as "small molecule". A quick perusal of the specification did not provide a definition for the above phrase thus rendering the claim unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening for a candidate bioactive agent capable of modulating PARP activity using a TaHo protein comprising a polypeptide encoded by polynucleotides SEQ ID NO:1 or 2, does not reasonably provide enablement for such a method using any or all proteins encoded by a polynucleotide that is 90% identical to SEQ ID NO:1 or 2 including variants, mutants and recombinants of such polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 27-30 are so broad as to encompass any polypeptide encoded by a polynucleotide that is 90% identical to SEQ ID NO:1 or 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims for the said method. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which

changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only two such polypeptides.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all polypeptides encoded by polynucleotides that are 90% identical to SEQ ID NO:1 or 2 because the specification does not establish: (A) all polypeptides encoded by polynucleotides that are 90% identical to SEQ ID NO:1 or 2 continue to encode polypeptides that have the same or identical activity as that of polypeptides encoded by SEQ ID NO:1 or 2; (B)regions of the protein structure (i.e., the proteins encoded by SEQ ID NO:1 or 2) which may be modified without effecting their specific (tankyrase or PARP) activity; (C) the general tolerance of tankyrases homologs to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological

function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all polypeptides encoded (irrespective of its activity) by polynucleotides that are 90% identical to SEQ ID NO:1 or 2 in the said method. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics for the above method is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 27-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 27-30 are directed to a method wherein polypeptides encoded by polynucleotides that are 90% identical to SEQ ID NO:1 or 2 are used. Claims 27-30 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of the polypeptide

encoded by the polynucleotides with SEQ ID NO:1 or 2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences encoded by polynucleotides that are 90% identical to SEQ ID NO:1 or 2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of function. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only two species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 27-30 are rejected under 35 U.S.C. 102(a)/(e) as being anticipated by Berthelsen et al. (US 6,455,290 B1, 9-24-2000, filed on 7-9-1999). This rejection is based upon the public

availability of a printed publication/patent. Claims 27-30 of the instant application are drawn to a method for screening for a candidate bioactive agent capable of modulating PARP activity comprising the steps of providing a TaHo protein, a candidate agent and a source poly ADP-ribose; and determining the amount of poly ADP-ribose associated with said TaHo protein wherein the TaHo protein is encoded by a nucleic acid having at least 90% identity to the nucleic acid sequence set forth in SEQ ID NO:1 or 2, wherein the bioactive agent is a small molecule or a peptide and wherein said source of poly ADP-ribose is selected from a group consisting of NAD, biotinylated NAD or radioactively labeled NAD. Berthelsen et al. disclose an identical method (see column 28, e.g. 8) and provide a protein called THP instead of TaHo wherein said protein is 99.1% identical to the protein encoded by SEQ ID NO:1 or 2 (see enclosed sequence alignments). Therefore the polynucleotide encoding said THP protein must be more than 90% identical to SEQ ID NO:1 or 2. The reference also discloses the use of small molecules for use as bioactive agents and the use of radiolabeled NAD as a source of poly ADP –ribose. Therefore, Berthelsen et al. anticipate claims 27-30 as written.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone

numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
April 14, 2003